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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,424	05/10/2005	Kaoru Miyamoto	47232.5003/00US	4728

55694 7590 10/18/2007

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,424	MIYAMOTO ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-12* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/2/2007, 7/14/2006, 5/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 5/10/2005, in which claim 3 was canceled, and claim 6 was amended. Currently, claims 1, 2 and 4-12 are pending.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 8/2/2007 is acknowledged.

Claims 7, 8 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/2/2007.

An examination on the merits of claims 1, 2, 4-6 and 9-11 follows.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt of the certified copy of the foreign priority document, Japan 2002-366512, is acknowledged. These papers have been placed of record in the file.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 7/14/2006 and 8/2/2007, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible

copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

In the instant case, the IDS filed 5/10/2005 cites WO 01/57190 and two non-patent literature references. WO 01/57190 has been cited on a PTO-892 and mailed herewith. Yamada et al, FEBS Lett., 1999 has been considered on the IDS filed 7/14/2005. Yamada et al, Biochem. Biophys. Res. Commun., 1999 has not been considered, because a copy of the reference was not provided.

Specification

The abstract of the disclosure is objected to because it is presented as two paragraphs instead of a single paragraph. Correction is required. See MPEP § 608.01(b).

The use of the trademark GENBANK (page 1, line 32; page 11, line 30; page 14, line 26) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting (Warning)

Applicant is advised that should claim 9 be found allowable, claim 10 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objections

Claims 1, 2, 4-6 and 9-11 are objected to because of the following informalities: the phrase "protein or peptide" is redundant. The specification does not define a protein to mean something different than a peptide, and thus both terms refer to a compound comprising two or more amino acid residues linked by a peptide bond. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-6 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the functional domain" in line 7. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear to which functional domain the claim refers. The sequence of SEQ ID NO: 1 comprises multiple different domains: zinc finger domains, homeodomains, glutamic acid-rich domain, dimerization domain, interaction domain with NF-YA, repression domain, and nuclear localization sequences (e.g., paragraph bridging pages 6-7; Figure 14).

Claim 2 depends from claim 1 and is thus indefinite due to lack of antecedent basis as applied to claim 1.

Claim 4 recites the limitation "the functional domain" in line 8. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear to which functional domain the claim refers. The sequence of SEQ ID NO: 1 comprises multiple different domains: zinc finger domains, homeodomains, glutamic acid-rich domain, dimerization domain, interaction domain with NF-YA, repression domain, and nuclear localization sequences (e.g., paragraph bridging pages 6-7; Figure 14).

Claims 5 and 6 depend from claim 4 and thus are indefinite due to lack of antecedent basis as applied to claim 4.

Claim 9 recites the limitation "the functional domain" in line 2. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear to which functional domain

the claim refers. The sequence of SEQ ID NO: 1 comprises multiple different domains: zinc finger domains, homeodomains, glutamic acid-rich domain, dimerization domain, interaction domain with NF-YA, repression domain, and nuclear localization sequences (e.g., paragraph bridging pages 6-7; Figure 14).

Claim 10 recites the limitation "the functional domain" in line 3. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear to which functional domain the claim refers. The sequence of SEQ ID NO: 1 comprises multiple different domains: zinc finger domains, homeodomains, glutamic acid-rich domain, dimerization domain, interaction domain with NF-YA, repression domain, and nuclear localization sequences (e.g., paragraph bridging pages 6-7; Figure 14).

Claim 11 depends from claim 10 and thus is indefinite for the same reason applied to claim 10.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-6, and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the

existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to drugs (claims 1 and 2), therapeutic products to treat hepatoma (claims 4-6), and proteins or peptides to repress transcription of genes expressed specifically in hepatoma cells (claims 10 and 11). The only disclosed use for the claimed produces is for the treatment of hepatoma by repressing genes specific to hepatoma (e.g., page 1, lines 4-5). Thus, the nature of the invention is complex in that the claimed proteins must be capable of repressing genes specific to hepatoma, such as type II hexokinase and pyruvate kinase M, in a manner sufficient to have a therapeutic effect.

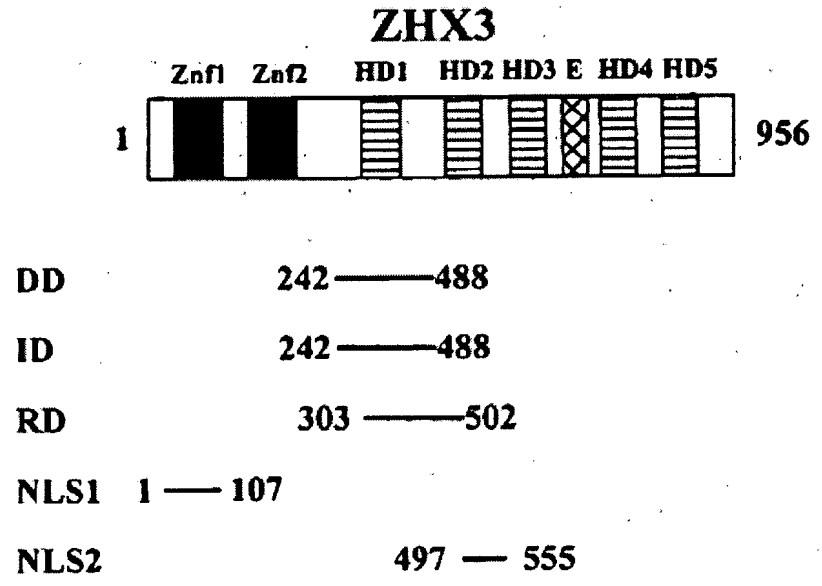
Breadth of the claims: The claims are broad in that they are drawn to or encompass a large genus of proteins: (1) a protein having an amino acid sequence (two or more contiguous amino acids) of SEQ ID NO: 1, (2) a protein having an amino acid sequence (two or more contiguous amino acids) of SEQ ID NO: 1, wherein the sequence comprises a deletion, substitution or addition of one or several amino acids with respect to the amino acid sequence of SEQ ID NO: 1 and wherein the protein has transcriptional repressor activity, (3) a protein comprising a functional domain of SEQ ID NO: 1, and (4) a protein comprising a functional domain of SEQ ID NO: 1, wherein the protein has a deletion, substitution or addition of one or several amino acid with respect to a functional domain of SEQ ID NO: 1, and wherein the protein has transcriptional repressor activity. The claims do not require the protein to have DNA binding activity and only require repressor activity, yet the protein is required to repress transcription of specific genes, such as type II hexokinase and pyruvate kinase M, and treat

hepatoma. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the specification and existence of working examples: The specification asserts that it is known in the prior art that pyruvate kinase M gene and type II hexokinase gene are genes for the glycolytic pathway that are specifically induced in hepatoma (e.g., page 1). The specification states that NF-Y is a common transcription factor for both genes but is not differentially expressed between normal liver and hepatoma cells (e.g., page 1). Further, the specification teaches that ZHX1 interacts with NF-Y and is ubiquitously expressed (e.g., page 1).

The present specification teaches the identification of ZHX3 (SEQ ID NO: 1), which is a protein that interacts with ZHX1. The ZHX 3 protein contains the following domains:

Figure 14



ZHX3 contains two zinc fingers, five homeodomains, a glutamic acid-rich region (E), a dimerization domain for heterodimerization with ZHX1 and homodimerization, an interaction

domain (ID) for interacting with NF-Y, a repression domain (RD), and nuclear localization sequences (NLS) (e.g., paragraph bridging pages 6-7; Figures 3, 6 and 14). The working examples of the specification demonstrate the ability of ZHX3 to interact with ZHX1 and NF-Y, the nuclear localization of ZHX3, and the ability of amino acids 303-502 to function as a transcriptional repression domain. As with ZHX1, ZHX3 is ubiquitously expressed (e.g., page 16, lines 17-22).

No working examples are provided that demonstrate the ability of any ZHX3 protein to treat hepatoma or to alter the expression of pyruvate kinase M gene or type II hexokinase gene in any model.

Predictability and state of the art: At the time the invention was made, it would have been an unpredictable venture to use a ZHX3 protein to treat hepatoma. There is no evidence on the record that ZHX3 expression is lost in hepatoma cell, nor is there evidence that provision of ZHX3 to hepatoma cells will result in any therapeutic effect, including the reduction of type II hexokinase and pyruvate kinase M. As disclosed in the present specification, the ZHX3 protein is a member of the ZHX family of proteins (e.g., page 2, lines 23-25). The post-filing art teaches that ZHX3 forms heterodimers with both ZHX1 and ZHX2 (Kawata et al. Gene, Vol. 323, pages 133-140, December 2003; e.g., Abstract; page 139, section 3.4). While the art is silent with regard to the expression and function of ZHX3 in hepatoma, the post-filing art teaches increased expression of ZHX2 in hepatoma (Zhang et al. Neoplasma, Vol. 54, No. 3, pages 207-211, 2007). Like ZHX1 and ZHX3, ZHX2 contains zinc fingers and homeoboxes and is a transcriptional repressor (Zhang et al, Abstract). Zhang et al studied the expression of ZHX2 protein in normal liver and 236 hepatocellular carcinoma (hepatoma, HCC) samples and found

that ZHX2 protein is not expressed in normal liver but is expressed in HCC, with higher levels of expression in stage III-IV compared with stage I-II (e.g., paragraph bridging pages 207-208; page 210, Discussion; Table 1; Figure 1). ZHX2 protein expression was significantly higher in HCC cases with metastasis than without (e.g., page 210, right column, 2nd full paragraph). Thus, ZHX2 protein may take part in hepatocellular carcinogenesis and progression (e.g., paragraph bridging pages 210-211). Given the related structure and function and the heterodimerization of the ZHX family of proteins, it would be unpredictable to use any ZHX family member, including ZHX3, to treat hepatoma.

Amount of experimentation necessary: The quantity of experimentation required to determine how to use any claimed proteins to treat hepatoma is large, as the skilled artisan cannot rely upon the limited guidance provided by the present specification and prior art. One would be required to perform a large amount of trial and error experimentation to determine if SEQ ID NO: 1, and any of its fragments and variants, are capable of treating hepatoma or reducing the expression of hepatoma specific genes. Given the probable role of ZHX2 in hepatoma carcinogenesis and progression it would be unlikely for the related ZHX3 protein to function to reduce carcinogenesis and progression.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1, 2, 4-6, and 9-11 are not considered to be enabled by the instant specification.

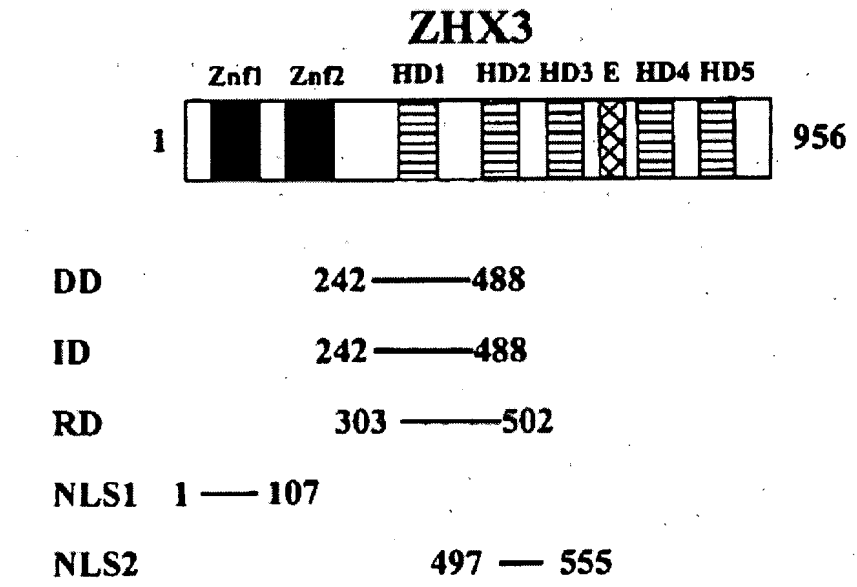
Claims 1, 2, 4-6 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a genus of proteins that (1) share "an amino acid sequence" with SEQ ID NO: 1, (2) comprise any number of amino acid deletions, substitutions, or additions relative to SEQ ID NO: 1 and have transcriptional repressor activity, (3) comprise a functional domain of SEQ ID NO: 1, (4) comprise any number of deletions, substitutions, or additions relative to a functional domain of SEQ ID NO: 1 and have transcriptional repressor activity. The use of the phrase "an amino acid sequence" in the claims only requires the claimed protein to have two or more contiguous amino acids in common with SEQ ID NO: 1. The only disclosed use for the claimed proteins is the treatment of hepatoma (e.g., page 1, lines 4-5). The rejected claims thus comprise a set of proteins that may or may not have repressor activity and must also act as a drug or therapeutic and regulate the expression of type II hexokinase and pyruvate kinase M.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes the amino acid sequence of SEQ ID NO: 1, which is the human ZHX3 protein. The working examples of the specification define fragments

100% identical to portions of SEQ ID NO: 1 that function as a dimerization domain (DD), interaction domain (ID) for interacting with NF-Y, a transcriptional repression domain (RD) and two nuclear localization sequences (NLS).

Figure 14



The working examples of the specification demonstrate the ability of ZHX3 to interact with ZHX1 and NF-Y, the nuclear localization of ZHX3, and the ability of amino acids 303-502 to function as a transcriptional repression domain. The repression domain (305-502) was able to reduce the level of expression of a reporter gene when operably linked to a Gal4 DNA binding domain (e.g., pages 19-20, Example 5; Figure 12) The specification does not teach that the repression domain (305-502) is capable of repressing transcription without being operably linked to a DNA binding domain. No description is provided of structure necessary to reduce the expression of type II hexokinase and pyruvate kinase M. Further, there is no evidence of record

that the ZHX3 protein is capable of treating hepatoma. There is no description of the specification of the structure necessary to treat hepatoma.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of different domains of the protein of ZHX3. The specific structure of ZHX3 is not related to the function of reducing the expression of type II hexokinase and pyruvate kinase M and thus one would not know how to vary the structure of the protein of SEQ ID NO: 1 and provide the claimed activities.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of proteins, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

"A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans

could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). In the instant case, the specification discloses the ZHX3 proteins of human (SEQ ID NO: 1) and rat (SEQ ID NO: 2) and teaches that they are 87.3% similar (e.g., 3, lines 4-10). However, it is unclear how the structure of ZHX3 in general relates to the function of modulating the expression of type II hexokinase and pyruvate kinase M and the treatment of hepatoma. Thus, if the full-length protein is capable of conferring these claimed properties, one cannot envision other structures that will have the same function.

Given the very large genus of proteins encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to structures necessary to regulate the expression of type II hexokinase and pyruvate kinase M and the treat hepatoma, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of proteins. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those proteins that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 1, 2, 4-6 and 9-11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 6 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al (WO 01/57190 A2; see the entire reference).

The claims are drawn to or encompass a protein or a peptide having "an amino acid sequence" of SEQ ID NO: 1. The phrase "an amino acid sequence" is reasonably interpreted as encompassing any two or more contiguous amino acids of SEQ ID NO: 1.

Tang et al teach that isolated polypeptides are separated from their natural source and contain, if anything, only a solvent, buffer, ion, or other component present in a solution (e.g., page 11, lines 19-24). Tang et al teach an isolated polypeptide of SEQ ID NO: 3447 (e.g., page 28, lines 9-34; page 338). The amino acid sequence of SEQ ID NO: 3447 is 99% identical to instant SEQ ID NO: 1 (see the attached alignment in Exhibit I). Because the amino acid sequence of SEQ ID NO: 3447 is 99% identical to the protein of SEQ ID NO: 1, it must contain a functional domain of the protein. Further, the high percent identity indicates that the protein of SEQ ID NO: 3447 would have the same function as instant SEQ ID NO: 1, such as the regulation of a type II hexokinase or pyruvate kinase M gene.

Claims 1, 2, 4, 5, 9 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Isogai et al (US Patent No. 6,943,241 B2; see the entire reference).

The claims are drawn to or encompass a protein or a peptide having "an amino acid sequence" of SEQ ID NO: 1. The phrase "an amino acid sequence" is reasonably interpreted as encompassing any two or more contiguous amino acids of SEQ ID NO: 1.

Isogai et al teach a purified polypeptide comprising the sequence of SEQ ID NO: 2005 (e.g., column 33, line 55 to column 34, line 53; Table 1 at column 6). The amino acid sequence of SEQ ID NO: 2005 is 100% identical to amino acids 300-956 of instant SEQ ID NO: 1 (see the attached alignment in Exhibit II).

As disclosed in the instant specification, amino acids 303-502 of SEQ ID NO: 1 represent a transcriptional repression domain. Thus, Isogai et al teach a protein or peptide comprising the functional domain of SEQ ID NO: 1, which has transcriptional repression activity.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

CELINE QIAN, PH.D.
PRIMARY EXAMINER

Exhibit I

<!--StartFragment-->RESULT 2
AAM78817
ID AAM78817 standard; protein; 956 AA.
XX
AC AAM78817;
XX
DT 06-NOV-2001 (first entry)
XX
DE Human protein SEQ ID NO 1479.
XX
KW Human; cytokine; cell proliferation; cell differentiation; gene therapy;
KW vaccine; peptide therapy; stem cell growth factor; haematopoiesis;
KW tissue growth factor; immunomodulatory; cancer; leukaemia;
KW nervous system disorder; arthritis; inflammation.
XX
OS Homo sapiens.
XX
PN WO200157190-A2.
XX
PD 09-AUG-2001.
XX
PF 05-FEB-2001; 2001WO-US004098.
XX
PR 03-FEB-2000; 2000US-00496914.
PR 27-APR-2000; 2000US-00560875.
PR 20-JUN-2000; 2000US-00598075.
PR 19-JUL-2000; 2000US-00620325.
PR 01-SEP-2000; 2000US-00654936.
PR 15-SEP-2000; 2000US-00663561.
PR 20-OCT-2000; 2000US-00693325.
PR 30-NOV-2000; 2000US-00728422.
XX
PA (HYSE-) HYSEQ INC.
XX
PI Tang YT, Liu C, Drmanac RT, Asundi V, Zhou P, Xu C, Cao Y;
PI Ma Y, Zhao QA, Wang D, Wang J, Zhang J, Ren F, Chen R, Wang ZW;
PI Xue AJ, Yang Y, Wejhrman T, Goodrich R;
XX
DR WPI; 2001-476283/51.
DR N-PSDB; AAK51950.
XX
PT Nucleic acids encoding polypeptides with cytokine-like activities, useful
PT in diagnosis and gene therapy.
XX
PS Claim 20; Page 3755-3757; 6221pp; English.
XX
CC The invention relates to polynucleotides (AAK51456-AAK53435) and the
CC encoded polypeptides (AAM78323-AAM80302) that exhibit activity elating to
CC cytokine, cell proliferation or cell differentiation or which may induce
CC production of other cytokines in other cell populations. The
CC polynucleotides and polypeptides are useful in gene therapy, vaccines or
CC peptide therapy. The polypeptides have various cytokine-like activities,
CC e.g. stem cell growth factor activity, haematopoiesis regulating
CC activity, tissue growth factor activity, immunomodulatory activity and
CC activin/inhibin activity and may be useful in the diagnosis and/or
CC treatment of cancer, leukaemia, nervous system disorders, arthritis and
CC inflammation. Note: Records for SEQ ID NO 2110 (AAK52581), 2111
CC (AAK52582) and 3666 (AAM80020) are omitted as the relevant pages from the
CC sequence listing were missing at the time of publication
XX
SQ Sequence 956 AA;

Query Match 99.9%; Score 4990; DB 4; Length 956;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 955; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 MASKRKSTTPCMIPVKTVVLQDASMEAQPAETLPEGPQQDLPPEASAASSEAAQNPSSTD 60
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Db          1 MASKRKSTTPCMIPVKTVVLQDASMEAQPAETLPEGPQQDLPPEASAASSEAAQNPSSTD 60

Qy         61 GSTLANGHRSTLDGYLYSCKYCDFRSHDMTQFVGHMNSEHTDFNKDPTFVCSGCSFLAKT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GSTLANGHRSTLDGYLYSCKYCDFRSHDMTQFVGHMNSEHTDFNKDPTFVCSGCSFLAKT 120

Qy        121 PEGLSLHNATCHSGEASFVWNVAKPDNHVVVEQSIPESTSTPDLAGEPSAEGADGQAEII 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 PEGLSLHNATCHSGEASFVWNVAKPDNHVVVEQSIPESTSTPDLAGEPSAEGADGQAEII 180

Qy        181 ITKTPIMKIMKGKAEAKKIHTLKENVPSQPVGEALPKLSTGEMEVREGDHSFINGAVPVS 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 ITKTPIMKIMKGKAEAKKIHTLKENVPSQPVGEALPKLSTGEMEVREGDHSFINGAVPVS 240

Qy        241 QASASSAKNPHAANGPLIGTVPVLPAGIAQFLSLQQQPPVHAQHHVHQPLPTAKALPKVM 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 QASASSAKNPHAANGPLIGTVPVLPAGIAQFLSLQQQPPVHAQHHVHQPLPTAKALPKVM 300

Qy        301 IPLSSIPTYNAAMDSNSFLKNSFHKFPYPTKAELCYLTVVTKYPEEQLKIWFTAQRLKQG 360
              |||||||||:||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 IPLSSIPTYSAAMDSNSFLKNSFHKFPYPTKAELCYLTVVTKYPEEQLKIWFTAQRLKQG 360

Qy        361 ISWSPEEIEDARKKMFNTVIQSVPQPTITVLNTPLVASAGNVQHLIQAALPGHVVGQPEG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 ISWSPEEIEDARKKMFNTVIQSVPQPTITVLNTPLVASAGNVQHLIQAALPGHVVGQPEG 420

Qy        421 TGGGLLVTQPLMANGLQATSSPLPLTVTSVPKQPGVAPINTVCSNTTSAVKVVNAAQSLL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TGGGLLVTQPLMANGLQATSSPLPLTVTSVPKQPGVAPINTVCSNTTSAVKVVNAAQSLL 480

Qy        481 TACPSITSQAFLDASIYKNKKSHEQLSALKGSFCRNQFPGQSEVEHLTKVTGLSTREVRK 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 TACPSITSQAFLDASIYKNKKSHEQLSALKGSFCRNQFPGQSEVEHLTKVTGLSTREVRK 540

Qy        541 WFSDRRYHCRNLKGSRAMIPGDHSSIIIDSVPEVSFSPSSKVPEVTCIPTTATLATHPSA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 WFSDRRYHCRNLKGSRAMIPGDHSSIIIDSVPEVSFSPSSKVPEVTCIPTTATLATHPSA 600

Qy        601 KRQSWHQTPDFTPTKYKERAPEQLRALESSFAQNPLPLDEELDRLRSETKMTRREIDSWF 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 KRQSWHQTPDFTPTKYKERAPEQLRALESSFAQNPLPLDEELDRLRSETKMTRREIDSWF 660

Qy        661 SERRKKVNAEETKKAEENASQEEEEAAEDEGGEEDLASELRVSGENGSLEMPSSHILAER 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SERRKKVNAEETKKAEENASQEEEEAAEDEGGEEDLASELRVSGENGSLEMPSSHILAER 720

Qy        721 KVSPIKINLKNLRVTEANGRNEIPGLGACDPEDDESNKLAEQLPGKVSCKKTAQQRHLLR 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 KVSPIKINLKNLRVTEANGRNEIPGLGACDPEDDESNKLAEQLPGKVSCKKTAQQRHLLR 780

Qy        781 QLFVQTQWPSNQDYDSIMAQTGLPRPEVVRWFGDSRYALKNGQLKWYEDYKRGNFPPGLL 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 QLFVQTQWPSNQDYDSIMAQTGLPRPEVVRWFGDSRYALKNGQLKWYEDYKRGNFPPGLL 840
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Qy          841 VIAPGNRELLQDYYMTHKMLYEEDLQNLCDKTQMSSQQVKQWFAEKMGEETRAVADTGSE 900
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          841 VIAPGNRELLQDYYMTHKMLYEEDLQNLCDKTQMSSQQVKQWFAEKMGEETRAVADTGSE 900

Qy          901 DQGPGTGELTAVHKGMGDTYSEVSENSESWEPRVPEASSEPFDTSSPQAGRQLETD 956
                |||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          901 DQGPGTGELTAVHKGMGDTYSEVSENSESWEPRVPEASSEPFDTSSPQAGRQLETD 956
<!--EndFragment-->
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Exhibit II

<!--StartFragment-->RESULT 1
US-10-104-047-2005
; Sequence 2005, Application US/10104047
; Patent No. 6943241
; GENERAL INFORMATION:
; APPLICANT: HELIX RESEARCH INSTITUTE
; TITLE OF INVENTION: No. 6943241el full length cDNA
; FILE REFERENCE: H1-A0105
; CURRENT APPLICATION NUMBER: US/10/104,047
; CURRENT FILING DATE: 2002-03-25
; PRIOR APPLICATION NUMBER:
; PRIOR FILING DATE:
; NUMBER OF SEQ ID NOS: 4096
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2005
; LENGTH: 657
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-104-047-2005

Query Match 68.6%; Score 3428; DB 2; Length 657;
Best Local Similarity 100.0%; Pred. No. 1.4e-285;
Matches 657; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy        300 MIPLSSIPTYNAAMDSNSFLKNSFHKFPYPTKAELCYLTVVTKYPEEQLKIWFTAQRLKQ 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MIPLSSIPTYNAAMDSNSFLKNSFHKFPYPTKAELCYLTVVTKYPEEQLKIWFTAQRLKQ 60

Qy        360 GISWSPEEIEDARKKMFNTVIQSVPQPTITVLNTPLVASAGNVQHLIQAALPGHVVGQPE 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GISWSPEEIEDARKKMFNTVIQSVPQPTITVLNTPLVASAGNVQHLIQAALPGHVVGQPE 120

Qy        420 GTGGGLLVTQPLMANGLQATSSPLPLTVTSVPKQPGVAPINTVCSNTTSAVKVVNAAQSL 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GTGGGLLVTQPLMANGLQATSSPLPLTVTSVPKQPGVAPINTVCSNTTSAVKVVNAAQSL 180

Qy        480 LTACPSITSQAFLDASIYKNKKSHEQLSALKGSFCRNQFPGQSEVEHLTKVTGLSTREVR 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 LTACPSITSQAFLDASIYKNKKSHEQLSALKGSFCRNQFPGQSEVEHLTKVTGLSTREVR 240

Qy        540 KWFSDRRYHCRNLKGSRAMIPGDHSSIIIDSVPEVSFSPSSKVPEVTCIPTTATLATHPS 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KWFSDRRYHCRNLKGSRAMIPGDHSSIIIDSVPEVSFSPSSKVPEVTCIPTTATLATHPS 300

Qy        600 AKRQSWHQTPDFTPTKYKERAPEQLRALESSFAQNPLPLDEELDRLRSETKMTRREIDSW 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 AKRQSWHQTPDFTPTKYKERAPEQLRALESSFAQNPLPLDEELDRLRSETKMTRREIDSW 360

Qy        660 FSERRKKVNAEETKKAEENASQEEEEAAEDEGGEEDLASELRVSGENGSLEMPSSHILAE 719
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Db        361 FSERRKKVNAEETKKAEENASQEEEEAAEDEGGEEDLASELRVSGENGSLEMPSSHILAE 420

Qy        720 RKVSPIKINLKNLRVTEANGRNEIPGLGACDPEDDESNKLAEQLPGKVSCKKTAQQRHLL 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 RKVSPIKINLKNLRVTEANGRNEIPGLGACDPEDDESNKLAEQLPGKVSCKKTAQQRHLL 480

Qy        780 RQLFVQTQWPSNQDYDSIMAQTGLPRPEVVRWFGDSRYALKNGQLKWYEDYKRGNFPPGL 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 RQLFVQTQWPSNQDYDSIMAQTGLPRPEVVRWFGDSRYALKNGQLKWYEDYKRGNFPPGL 540

Qy        840 LVIAPGNRELLQDYYMTHKMLYEEDLQNLCDKTQMSSQQVKQWFAEKMGEETRAVADTGS 899
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Db         541 LVIAPGNRELLQDYYMTHKMLYEEDLQNLCDKTQMSSQQVKQWFAEKMGEETRAVADTGS 600

Qy         900 EDQGPGTGELTAVHKGMGDTYSEVSENSESWEPRVPEASSEPFDTSSPQAGRQLETD 956
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         601 EDQGPGTGELTAVHKGMGDTYSEVSENSESWEPRVPEASSEPFDTSSPQAGRQLETD 657

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